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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,724	09/25/2003	W. Edward Robinson JR.	UCI-12094	8496

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EXAMINER	
HUYNH, CARLIC K	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
03/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/672,724	ROBINSON ET AL.	
	Examiner	Art Unit	
	CARLIC K. HUYNH	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-32* is/are pending in the application.

4a) Of the above claim(s) *31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks filed on November 13, 2007 is acknowledged.

Status of the Claims

1. Claims 28-32 are pending in the application, with claims 31-32 having been withdrawn in response to the restriction requirement submitted on February 23, 2007. Accordingly, claims 28-30 are being examined on the merits herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirsch et al. (The New England Journal of Medicine, 1993, Vol. 328, No. 23, pp. 1686-1695) in view of Robinson et al (Proceedings of the National Academy of Sciences of the United States of America, 1996, Vol. 93, pp. 6326-6331).

Hirsch et al. teach treatment of HIV infection with zidovudine, which is also known as AZT (abstract). Hirsch et al. further teach resistance to zidovudine (page 1688). Hirsch et al. also teach using combination therapy because of problems related to drug failure and resistance and agents used in combination therapy target the different stages in the replicative cycle of HIV,

including targeting the integration of HIV DNA with integrase inhibitors (page 1691 and Table 1). The combination therapy taught by Hirsch et al. employ the use of zidovudine and a protease inhibitor or zidovudine and another reverse transcriptase inhibitor e.g. didanosine (page 1691).

Hirsch et al. do not teach combination therapy with integrase inhibitors. In fact, Table 1 acknowledges that no integrase inhibitors were discover at the time of publication (Table 1).

Robinson et al. teach integrase inhibitors and that integrase inhibitors can be used to treat HIV (abstract).

Accordingly, absence the showing of unexpected results, it would have been obvious to a person of skill in the art at the time of the invention to employ zidovudine of Hirsch et al. to be used with integrase inhibitors to treat HIV infection because the compounds of Robinson et al. teach integrase inhibitors and according to Hirsch et al. and Robinson et al., zidovudine can be used in a combination therapy and integrase inhibitors can be used in combination therapy for treating HIV infection.

The motivation to combine the compounds of Hirsch et al. to the compounds of Robinson et al. is that the compounds of Robinson et al. can be used in a combination therapy to treat HIV infection.

It is noted that "It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose" and "It is obvious to combine two compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose". *In re Kerkhoven*, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

Regarding at least partially resistant and highly resistant as recited in claims 28-29, it is noted that Hirsch et al. teach resistance can develop in long term therapy with zidovudine (page 1688). Since Hirsch et al. teach merely resistance to zidovudine, it is obvious that the degree of resistance to zidovudine is addressed. Thus, Hirsch et al. teaches at least partially resistant and highly resistant as recited in instant claims 28-29.

Response to Arguments

3. Applicant's arguments, see "Remarks" filed on November 13, 2007, with respect to "Obviousness Rejection" to claims 28-30 has been fully considered and are not persuasive.

Applicants argue that the instant claims include the limitation of "a patient having an HIV infection that is at least partially resistant to treatment by said reverse transcriptase inhibitor". Moreover, Applicants argue the Hirsch et al. (The New England Journal of Medicine, 1993, Vol. 328, No. 23, pp. 1686-1695) do not teach treating a patient partially resistant to a reverse transcriptase inhibitor with the same reverse transcriptase inhibitor in combination with other agents. In fact, Applicants cite Japour (AIDS Clinical Care, 1995, Vol. 7, No. 8, pp. 63-65 and 67), which disclose "continued treatment in the face of AZT resistance may be like no treatment at all", as further evidence that their invention is not obvious to the skilled artisan. Applicants also argue that Hirsch et al. do not teach a synergistic effect of the reverse transcriptase inhibitor and the protease inhibitor.

Examiner disagrees. Applicants' attention is directed to Hirsch et al. where combination therapy of reverse transcriptase resistant HIV targets different stages in the replicative cycle of the virus (e.g. zidovudine and a protease inhibitor) or the same stage (e.g. zidovudine and

didanosine) (page 1691). Thus the patient population of Hirsch et al. may be a zidovudine resistant HIV patient that can be treated with combination therapy, either with zidovudine and a protease inhibitor or zidovudine and didanosine. Hirsch et al. thus teach combination therapy with either different reverse transcriptase inhibitors or a reverse transcriptase inhibitor and a protease inhibitor. Examiner notes that the Japour reference cited by Applicants only addresses reverse transcriptase resistant HIV patients treated with combination therapy of different dideoxynucleoside agents and not combination therapy with reverse transcriptase inhibitors and protease inhibitors.

Examiner also points that it would be obvious to the skilled artisan that Hirsch et al. teach a synergist effect. The reverse transcriptase resistant patient, regardless of the degree of resistance, would not respond as well to treatment with the same reverse transcriptase inhibitor he or she is resistant to. If that patient is treated with the same reverse transcriptase inhibitor he or she is resistant to **and** another drug, such as a protease inhibitor, there would be an inherent synergist effect on HIV, namely the minimal effect by the reverse transcriptase inhibitor that the patient is resistant to **and** the effect of the protease inhibitor, which targets a different stage of the replicative cycle of the virus. As a result, the treatment with reverse transcriptase inhibitor and a protease inhibitor would have an additive inhibitory effect on HIV since the protease inhibitor targets a different stage of the viral replicative cycle, a stage that the HIV patient has not developed resistance.

Thus, the Rejections under 35 U.S.C. § 103 to claims 28-30 have been maintained.

Conclusion

4. No claims are allowable.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carlic K. Huynh whose telephone number is 571-272-5574. The examiner can normally be reached on Monday to Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612

ckh